Original Article

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Microbial Profile and Antibiotic Sensitivity Pattern in Urinary Tract Infections among Children Attending a Tertiary Care Center, Idukki District, Kerala: A Cross-sectional Study

Paediatrics Section

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ABSTRACT

Introduction: Over the recent decades, the importance of Urinary Tract Infections (UTI) has been increasingly recognised in children. The occurrence of UTI during childhood may lead to acute and/or chronic consequences, such as impaired renal function, renal scarring, and hypertension. Due to the irrational use of antimicrobials, multidrug resistant bacterial strains are frequent. Hence, there is an urgent need for continuous surveillance of the microbiological profile of UTI.

Aim: To investigate the microbial profile and antibiotic sensitivity pattern from the urine of paediatric patients suspected to have UTI in Idukki district, Kerala and to explore its association with seasonal variations.

Materials and Methods: This clinical cross-sectional study was conducted in Al Azhar Medical College and Super Specialty Hospital, Thodupuzha, Idukki, Kerala, India, from January 2019 to December 2021. The study involved 882 paediatric patients in the age group 0-15 years with symptoms and signs suggestive of UTI. Data regarding age, gender, season, laboratory and culture results, and antibiotic sensitivity pattern were considered as variables of interest. Analysis was performed using mean and standard deviation for quantitative variables, and frequency and proportion for categorical variables. The statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) version 20.0 and Microsoft Excel 2010.

Results: The study involved 882 patients, of which 399 were males (45.2%) and 483 were females (54.8%) with a male-to-female ratio of 0.8:1. The mean age of patients was four years, and a peak incidence was observed in children in the age group of 1-3 years, with 333 (37.8%) children. Microbial growth was observed in the urine of 325 (36.8%) patients. After excluding normal commensal perineal flora and insignificant bacteriuria, 233 samples had significant growth, with males accounting for 106 (45.5%) and females 127 (54.5%). The male-to-female ratio was 0.8 to 1. These samples mostly exhibited growth of aerobic bacteria (232, 99.6%) and *Candida albicans* (1, 0.4%). *E. coli* (106, 45.5%) was identified as the most predominant aetiological agent for paediatric UTI.

Conclusion: The results of this study suggest that it would be advisable for paediatricians in Idukki district to refrain from using Ampicillin to treat cases suspected to have UTI. Preventive measures should be advised to all patients, with emphasis on urinary hygiene during the monsoon and winter seasons.

Keywords: Antimicrobial, *Escherichia coli*, Multidrug resistant, Paediatric, *Staphylococcus aureus*

INTRODUCTION

The UTI is one of the most common infections among children. The risk of developing a UTI in childhood is approximately 1-3% in boys and 3-10% in girls [1]. UTI is defined as the growth of a significant number of organisms, i.e., more than 100,000 Colony-Forming Units (CFU)/mL of a single species in the urine sample in the presence of symptoms [2,3]. Timely and effective management of UTI with appropriate antibiotic administration is of immense importance to reduce the risk of long-term consequences in children [4].

A diagnosis of UTI is usually missed in infants and young children, as urinary symptoms are minimal and often non-specific in this age group. In children less than two years old, UTI is an important cause for fever without a focus. In neonates, it is usually a part of septicemia and can present with symptoms of fever, vomiting, lethargy, jaundice, and seizures. The typical presenting features in infants and young children include repeated fever, abdominal discomfort and pain, poor weight gain, and frequently, vomiting and diarrhoea. Among older children, the characteristic presenting features include dysuria, frequency, urgency, fever, and abdominal or flank pain. Adolescents may have symptoms restricted to the lower tract, and fever may not be present [2].

Previous similar studies from Kerala have described the microbial profile and pattern of antibiotic susceptibility from the northern, western, and eastern parts of Kerala [5-7]. However, there is a need to determine whether empirical antibiotics that are being prescribed by paediatricians in Idukki district for paediatric UTI as part of standard practice are still relevant in the era of increasing antibiotic resistance and effective for this condition or are contributing to greater antibiotic resistance in the region. Additionally, there is currently no literature from Idukki district providing information on the microbial profile of UTI and any correlation with seasonal variations. Thus, this study will help guide clinicians in this geographical area towards more effective prescription of antibiotics and will also fill the remaining gaps in microbiological data from the central part of Kerala.

Hence, this study was conducted to determine the microbial profile and antibiotic sensitivity pattern in UTI from the urine of paediatric patients suspected to have UTI in Idukki district, Kerala, and also to find its correlation with seasonal variations.

MATERIALS AND METHODS

This clinical cross-sectional study was conducted from January 2019 to December 2021 at Al Azhar Medical College and Super Specialty Hospital, Thodupuzha, a tertiary care teaching hospital in Idukki district. The study was approved by the Institutional Ethical Committee (IEC No: AAMC/IEC/2018-2019/10). Informed consent

was obtained from the parents or guardians of all patients before enrolling them in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Inclusion criteria: The study included 882 paediatric patients in the age group 0-15 years in the department of paediatrics with symptoms and signs suggestive of UTI [2] and had pyuria in the urine microscopy as per the Indian Society of Paediatric Nephrology Guidelines 2011 [8]. Only the samples which showed significant monobacterial growth (>10^5 CFU/mL) were confirmed as the UTI cases [8,9]. Only a single positive culture per patient was included in the analysis.

Exclusion criteria: Patients who were on any antibiotics (either oral or systemic) in the previous five days before presentation were excluded from the study.

A total of 882 samples, who presented in the Department of Paediatrics with symptoms and signs suggestive of UTI within the study duration, were enrolled in the study by convenience sampling.

Procedure

Data collection: Age, gender, seasonal variations, laboratory and culture results, and antibiotic sensitivity patterns were considered as variables of interest. Occurrence of seasonal variation of UTI with the prevalent seasons in Idukki district was also assessed. Urine samples (at least 10 mL) were obtained by either of the following methods: midstream clean catch, bladder catheterisation, or suprapubic aspiration. The collected specimens were transported immediately to the microbiology laboratory for further processing.

All samples were observed under the microscope for pyuria and were cultured on blood agar and MacConkey agar by the semi-quantitative method by streaking using a sterile calibrated wire loop and incubated aerobically for 18-24 hours at 35-37°C. Isolation and identification were done based on their morphology in Gram staining, cultural characteristics, and biochemical reactions [3,10]. Antimicrobial Susceptibility Testing (AST) was performed using the Kirby Bauer disk diffusion method as described by the Clinical Laboratory Standard Institute (CLSI) guidelines- 2012 [11,12].

According to the Kerala Meteorological Department [13], the seasons in Idukki are divided into three: summer (March-May), monsoon (June-October), and winter (November-February).

STATISTICAL ANALYSIS

All collected data were analysed and stored in a Microsoft Excel sheet. The analysis of all the parameters was done using mean and standard deviation for quantitative variables, and frequency and proportion for categorical variables. The statistical analyses were performed using Statistical Package for Social Science software SPSS version 20.0, (IBM Corp., Armonk, NY, USA) and Microsoft Excel 2010.

RESULTS

This was a prospective observational study involving 882 paediatric patients, conducted in a tertiary care teaching hospital in Idukki, Kerala. Out of these, 399 were males (45.2%) and 483 were females (54.8%) with a male: female ratio of 0.8:1. The mean age of patients was 3.45±1.25 years, and the peak age group for whom urine samples were sent for culture were children in the age group of 1-3 years {333 (37.8%)}.

Microbial growth was seen in the urine of 325 (36.8%). After excluding normal commensal perineal flora and insignificant bacteriuria among 92 subjects, 233 patient samples were taken-up for the study. Of these, males were 106 (45.5%), and females 127 (54.5%) {(male:female ratio of 0.8 to 1)}. Infants accounted for 100 cases (42.9%), 107 (45.9%) cases in the age group 1-5 years, 23 (9.9%) cases from the ages 6-10 years, and 3 cases (1.3%) were from older children [Table/Fig-1].

Out of the total 233, the specimens grew mostly aerobic and facultatively anaerobic bacteria {232 (99.6%)}, and fungi {1 (0.4%)}. *E. coli* {106 (45.5%)} was identified as the most predominant aetiological agent for paediatric UTI. This was followed by *Staphylococcus aureus* (considering both methicillin-resistant and methicillin-sensitive forms) {47 (20.2%)}, *Klebsiella* spp {29 (12.5%)}, *Enterococcus* spp {15 (6.4%)}, *Proteus* spp {12 (5.1%)}, *Streptococcus* spp {6 (2.6%)}, *Citrobacter* spp {6 (2.6%)}, and *Pseudomonas aeruginosa* {4 (1.7%)}. The aetiological agents occurring least in the present study were *Enterobacter* spp. {3 (1.3%)}, *Acinetobacter* {2 (0.9%)}, and one case each {1 (0.4%)} of *Morganella morganii*, *Staphylococcus saprophyticus*, and *Candida albicans* [Table/Fig-2].

Age group	Culture positive			Culture negative		
	Male	Female	Total (n%)	Male	Female	Total (n%)
0-12 months	59 (18.1%)	65 (20%)	124 (38.15%)	53 (9.52%)	47 (8.44%)	100 (17.95%)
1-5 (years)	61 (18.7%)	94 (28.9%)	155 (47.69%)	141 (25.31%)	175 (31.42%)	316 (56.73%)
6-10 (years)	12 (3.6%)	28 (8.6%)	40 (12.31%)	52 (9.34%)	55 (9.87%)	107 (19.21%)
11-15 (years)	2 (0.6%)	4 (1.2%)	6 (1.85%)	19 (3.41%)	15 (2.69%)	34 (6.1%)
TOTAL	134 (41.23%)	191 (58.7%)	325 (100%)	265 (47.58%)	292 (52.42%)	557 (100%)

[Table/Fig-1]: Age- and genderwise distribution of patient samples.

Organism	No. of cases
Aerobic bacteria (99.6%)	
E. coli	106 (45.5%)
Staphylococcus aureus	47 (20.2%)
Klebsiella spp.	29 (12.5%)
Enterococcus spp.	15 (6.4%)
Proteus spp.	12 (5.1 %)
Citrobacter spp.	6 (2.6%)
Streptococcus spp.	6 (2.6%)
Pseudomonas aeruginosa	4 (1.7%)
Enterobacter spp.	3 (1.3%)
Acinetobacter spp.	2 (0.9%)
Morganella morganii	1 (0.4%)
Staphylococcus saprophyticus	1 (0.4%)
Fungi (0.4%)	
Candida albicans	1 (0.4%)
Total	233

[Table/Fig-2]: Different types of organisms isolated from the urine samples of patients suspected to have UTI.

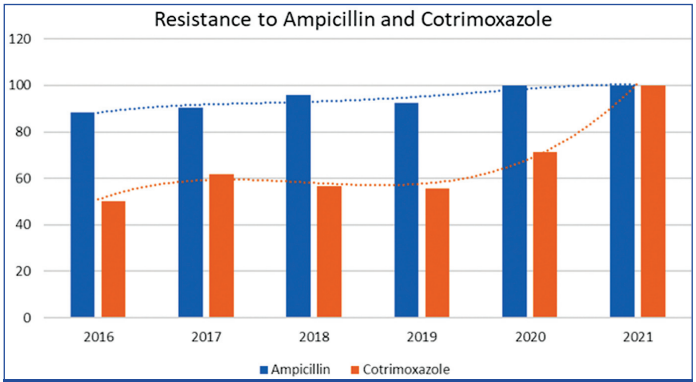
Antimicrobial Susceptibility Test (AST) for the isolated species showed that Amikacin and Piperacillin-Tazobactam were the most effective drugs, followed by Gentamicin, Ciprofloxacin, Cotrimoxazole, Ceftriaxone, and Ampicillin. *E. coli*, the most common pathogen identified, showed the highest susceptibility to Amikacin and the highest resistance to Ampicillin. *Staphylococcus aureus*, the second most common organism isolated, showed the

highest susceptibility to Piperacillin-Tazobactam, Ciprofloxacin, and the highest resistance to Cotrimoxazole [Table/Fig-3].

In the present study, most cases of UTI were seen during the monsoon season {117 (50.2%)} and winter {66 (28.3%)}, while the least were in the summer {50 (21.5%)} season. The authors studied the general trend of susceptibility of *E. coli* cultured from urinary samples to Ampicillin and Cotrimoxazole (oral first-line antibiotics included in this study, which are commonly prescribed in the outpatient setting) over a 6-year period from 2016 to 2021 and found a marked increase in the resistance of *E. coli* to both. This is a cause for concern in the local context and warrants continuous microbiological monitoring of urinary samples to help guide paediatricians towards better antibiotic prescribing practices [Table/Fig-4].

Organism	No. of cases	Ampicillin	Cotrimoxazole	Ciprofloxacin	Ceftriaxone	Gentamicin	Amikacin	Piptaz
E. coli	106 (45.5%)	8 (7.5%)	45 (42.4%)	61 (57.5%)	40 (37.7%)	86 (81.1%)	93 (87.7%)	79 (74.5%)
Staphylococcus aureus	47 (20.2%)	19 (40.4%)	17 (36.1%)	23 (48.9%)	21 (44.7%)	20 (42.5%)	21 (44.7%)	23 (48.9%)
Klebsiella spp	29 (12.5%)	0 (0 %)	18 (62.1%)	20 (68.9%)	10 (34.5%)	21 (72.4%)	24 (82.8%)	21 (72.4%)
Enterococcus spp	15 (6.4%)	7 (46.7%)	0 (0 %)	3 (20%)	0 (0 %)	6 (40%)	5 (33.3%)	7 (46.7%)
Proteus spp	12 (5.1%)	6 (50%)	10 (83.3%)	11 (91.7%)	12 (100%)	11 (91.7%)	11 (91.7%)	6 (50%)
Citrobacter spp	6 (2.6%)	0 (0 %)	3 (50%)	3 (50%)	3 (50%)	3 (50%)	6 (100%)	3 (50%)
Streptococcus spp	6 (2.6%)	5 (83.3%)	5 (83.3%)	3 (50%)	6 (100%)	3 (50%)	3 (50%)	3 (50%)
Pseudomonas aeruginosa	4 (1.7%)	0 (0 %)	0 (0 %)	1 (25%)	0 (0 %)	4 (100%)	4 (100%)	4 (100%)
Enterobacter spp	3 (1.3%)	0 (0 %)	3 (100%)	2 (66.7%)	1 (33.3%)	2 (66.7%)	2 (66.7%)	3 (100%)
Acinetobacter	2 (0.9%)	0 (0 %)	1 (50%)	2 (100%)	1 (50%)	1 (50%)	1 (50%)	2 (100%)
Morganella morganii	1 (0.3%)	0 (0 %)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)
Staphylococcus saprophyticus	1 (0.3%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)

[Table/Fig-3]: Antibiotic sensitivity of organisms cultured in the study population.



[Table/Fig-4]: Resistance trends to Ampicillin and Cotrimoxazole, which are among first line oral antibiotics commonly prescribed in the outpatient setting.

DISCUSSION

Available literature shows that about 80% of uncomplicated UTIs are caused by *Escherichia coli*, and additional causative organisms include *Staphylococcus saprophyticus*, *Klebsiella* pneumoniae, *Proteus* spp, *Pseudomonas aeruginosa*, and *Enterococcus* spp. Complicated or nosocomial infections are caused by organisms such as *E. coli*, *Proteus spp., K. pneumoniae*, *Enterobacter* spp., *P. aeruginosa, Staphylococcus*, and *Enterococcus* [5]. The present study identified *E. coli* as the most common organism isolated from the urinary cultures obtained, which is in tandem with the observations made by previous authors [6,7].

A female predominance was observed in this study, which is similar to the findings in previous studies by Ramgopal G and Shaji S et al., [2,5]. Even though anaerobes are thought to play a pathogenic role in UTI, the authors did not isolate them from any of our samples as the focus was more on aerobic culture. The large variability in their isolation rates among different studies may be due to differences in sampling and processing techniques, prior use of antibiotics, and differences in the timing of sampling during the course of the disease [11].

Antibiotic resistance has become a major clinical problem worldwide and has been increasing over the years [9]. In the present study, the most common organism causing UTI was found to be *E. coli*, which showed maximum susceptibility to Amikacin and maximum resistance to Ampicillin. This was similar to the findings in previous studies by Patwardhan V et al., and Shailaja TS and Mohankumar A [4,6]. Additionally, nearly half of the isolates of *E. coli* were resistant to fluoroquinolones, while more than half were resistant to cephalosporins. This is very worrisome, as these groups of antibiotics are used extensively in the treatment for UTI (though fluoroquinolones are not generally used in the paediatric population). This was similar to the findings by Patwardhan V et al., and Jitendranath A et al., [4,9].

Seasonal infectious diseases have been variously attributed to changes in various atmospheric conditions and the behaviour of the host. No previous study has evaluated the relation between seasonal changes and the bacteriology of UTI in Kerala. In this study, most cases of UTI were seen during the monsoon (149, 45.8%) and winter (106, 32.6%) seasons, while the least were in the summer (70, 21.5%) season.

The authors searched for similar studies in the English literature from Kerala, India, and found only four studies, one each from the districts of Kasargod (Northern Kerala) by Shaji S et al., Ernakulam (western Kerala) by Shailaja TS and Mohankumar A and Palakkad (Eastern Kerala) by Kallyadan VN [5-7]. The present study was conducted in Idukki district, which is situated in the central part of Kerala. The populations included in these studies consisted of paediatric patients alone (Kasargod and Ernakulam) and both (Palakkad). All four studies showed *E. coli* as the most common organism causing UTI, with maximum sensitivity to Imipenem and Nitrofurantoin in the study conducted in Kasaragod, Meropenem in the study conducted in Ernakulam, and Amikacin in the study conducted in Palakkad and Idukki. On the other hand, maximum resistance was found to Ampicillin and Amoxicillin in the study conducted in Kasaragod, Ampicillin/Sulbactam and Cefixime in the study conducted in Ernakulam, and Ampicillin in the study conducted in Palakkad and Idukki [Table/Fig-5].

The authors in the present study also searched for similar studies in the English literature from other parts of India over the period of

Author, Year	District of Kerala	Population (age group)	Study duration	No. of bacterial culture positive samples	Most common organisms cultured	Maximum antibiotic sensitivity	Maximum antibiotic resistance	Seasonal variation
Kallyadan V et al., [7] (2017)	Kasaragod	Paediatric (3 months to 18 years)	3 years	523	*E. coli*	Imipenem Nitrofurantoin	Ampicillin Amoxicillin	-

Shaji S et al., [5] (2021)	Kochi	Paediatric (age <18 years)	2 year	144	*E. coli*	Meropenem	Ampicillin/sulbactum Cefixime	-
Shailaja TS and Mohankumar A [6] (2017)	Palakkad	Both adult (≥15 years) and paediatric (<15 years)	1 year	1265 (33.5%)	*E. coli*	Amikacin	Ampicillin	-
Present study (2022)	Idukki	Paediatric (1 month to 18 years)	3 years	325 (36.8%)	*E. coli*	Amikacin	Ampicillin	Maximum cases in monsoon (42.6%)

[Table/Fig-5]: Comparison of UTI microbiological studies from Kerala, India [5-7].

2019-2023 and found five studies [14-18]. The studies were from West Bengal, Odisha, Jammu and Kashmir, Haryana, Tamil Nadu, and Delhi. The study from West Bengal by Chakraborty M et al., was conducted over a period of 10 months among paediatric ICU patients and obtained 18 positive cultures, with maximum sensitivity towards Carbapenems and Amikacin and maximum resistance to Cephalosporins, with the most common organism isolated being *Klebsiella* [14]. Whereas, the study from Odisha by Acharya NC et al., was conducted over a year among children less than 13 years of age, showing 186 positive cultures having maximum sensitivity towards Nitrofurantoin [16]. The study from Jammu and Kashmir by Kawoosa K et al., was conducted among children less than 3 years of age over a year with 216 positive cultures showing maximum sensitivity towards Amikacin and Nitrofurantoin [17]. The study from Haryana by Gupta MS et al., was also conducted over a year among children less than 5 years, with 200 positive cultures with the maximum sensitivity towards Piperacillin/Tazobactam [18].

On the other hand, a study from Delhi by Perween N et al., was carried out among the age group of 6 months to 18 years over 2 years and obtained 614 positive cultures, showing maximum sensitivity towards Colistin, Nitrofurantoin, and Amikacin, and maximum resistance to Ampicillin [15]. Lastly, the study from Tamil Nadu by Typhena C et al., was conducted over five years and involved children less than 15 years of age, obtaining 331 positive cultures with maximum sensitivity towards Nitrofurantoin and Cefpodoxime, and maximum resistance towards Co-trimoxazole [Table/Fig-6] [1,14-18].

Author, Year	Location	Population	Duration	Positive cultures	Maximum antibiotic sensitivity	Maximum antibiotic resistance
Chakraborty M et al., [14], 2023	West Bengal	Paediatric ICU patients	10 months	18	Carbapenems, Amikacin	Cephalosporins
Perween N et al., [15], 2022	Delhi	6m - 18 years	2 years	614	Colistin, Nitrofurantoin, Amikacin	Ampicillin
Typhena C et al., [1], 2021	Tamil Nadu	<15 years	5 years	331	Nitrofurantoin, cefpodoxime	Co-trimoxazole
Acharya NC et al., [16], 2021	Odisha	<13 years	? 1 year	186	Nitrofurantoin	-
Kawoosa K et al., [17], 2019	Jammu and Kashmir	<3 years	1 year	216	Amikacin, Nitrofurantoin	-
Gupta MS et al,m [18], 2019	Haryana	<5 years	1 year	200	Pipercilline/tazobactam	-
Present study (2022)	Idukki	Paediatric (1 month to 18 years)	3 years	325 (36.8%)	Amikacin	Ampicillin

[Table/Fig-6]: Comparison of paediatric UTI microbiograms in different regions of India from 2019-2023 [1,14-18].

Seasonal variation in the occurrence of UTI was not discussed in any of the other studies conducted in Kerala. Hence, we could not compare it with our study, which showed the maximum cases in the monsoon season {149 (45.8%)} and the minimum in the summer season {70 (21.5%)}. A study from Belgium by Boon HA et al., regarding incidence rates and trends of childhood UTIs found that, apart from gender and age considerations, the rates of cystitis tracked a distinct pattern of seasonality (p<0.001), with the period from June to August showing a slight decrease in incidence [19]. Similarly, further studies in India to evaluate the importance of weather as an environmental factor favouring the occurrence of UTIs would help guide clinicians to have a high degree of clinical suspicion when evaluating these patients during those particular seasons.

Limitation(s)

The limitations of the study are that the study was restricted to a single center, only including patients visiting the hospital, and the UTI in the community was not well-assessed. There was non-uniformity in collecting urine samples and a lack of data on clinical response and outcomes. As this study focused on the burden of antimicrobial resistance, the clinical presentations have not been described.

CONCLUSION(S)

The results of this study suggest that it would be wise for paediatricians in Idukki district to refrain from using Ampicillin empirically to treat cases suspected to have UTI. Also, more and more strains of common uropathogens are becoming resistant to commonly used urinary antibiotics like cotrimoxazole, cephalosporins, and fluoroquinolones. This translates to increased use of higher antibiotics and consequent cost to the patient, as well as increased morbidity to the patient and consumption of healthcare resources, which may be put to better use in the community. Preventive measures should be advised to all patients, with an emphasis on urinary hygiene in the monsoon and winter seasons. Therefore, it is imperative to tailor the treatment of patients with UTI based on culture and sensitivity reports in order to optimise the therapy and reduce treatment failures and their sequelae.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
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- Financial or Other Competing Interests: None
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